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To: . E. B. Sanders
From: . H. J. Grubbs
Subject: . Plans and Objectives (Project 2525)

Date: October 30, 1981

General Objectives:

The general objective of Charge Number 2525 is to elucidate the chemistry which takes place on a cigarette during smoking. Programs have been developed which complement, rather than overlap those programs being pursued in Charge Number 2501. These programs and their objectives are:

1. Synthesis of radiolabelled, stable isotope labelled, or unlabelled materials for use in precursor-product relationships. These materials will be utilized to study thermal reactions which are likely to produce either undesirable or desirable products. Unlabelled compounds prepared to investigate the formation of desirable products will also be investigated directly.
2. Development and application of radioanalytical methodology to conduct precursor-product studies in situations where non-volatile products are formed. Such methodology will address the problems delineated above in uses where gas chromatographic techniques are not useful.
3. Isolation of specific substances from complex mixtures. Two purposes will be served by this endeavor. The first involves the isolation of radiolabelled natural products, obtained from chamber grown plants, to serve as starting materials in precursor-product studies. The second involves isolation and identification of products formed from model chemical reaction studies (see Item 4).
4. Smoke chemistry modelling studies. The end point of smoke precursor-product studies is the identification of a specific precursor for specific products. Such a study provides no information which would enable one to either increase or decrease (if not eliminate) certain products derived from a specific precursor except by total removal of the precursor which is rarely

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possible. We plan to initiate a program wherein the detailed chemistry of the product-precursor conversion will be studied in order to attempt to discover procedures which can be utilized to alter this conversion on a burning cigarette.

In order to accomplish these general objectives, the following specific projects will be pursued.

Aza-Arene Program

1. To delineate the alkaloid production of ^{14}C -labelled tobacco plants with regard to both quantities and percentages of tobacco alkaloids produced. (Complete 1st Quarter)
2. To isolate and purify (to 99.99% purity) multi-gram quantities of ^{14}C -nicotine(U). (Complete 2nd Quarter)
3. To develop techniques to fractionate WSC for total removal of ^{14}C -nicotine(U) and simple (small) radiolabelled fragments of nicotine. (Complete 2nd Quarter)
4. To develop techniques for the isolation and radiochemical characterization of an aza-arene sub-fraction. (Complete 4th Quarter)

Natural Products Chemistry

1. To continue the isolation of ^{14}C -natural products from tobacco (or other suitable plant materials). Areas of interest are tobacco leaf glycosides, terpenes, structural carbohydrates, and amino acid/proteins. (Ongoing)
2. To develop alternate methods of obtaining ^{14}C -nicotine(U) with higher specific activity. A first approach is to explore the use of tobacco tissue culture (callus tissues). (Start 2nd Quarter)
3. To complete the isolation, identification, quantitation, and supply of samples of the anti-feedant azadiractin to Project 1101. (Complete 1st Quarter)

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4. To isolate and characterize additional quantities of rutin for product-precursor studies. (Complete 3rd Quarter)
5. To render technical assistance to outside projects when compatible with the accomplishment of our primary objectives. (Tonka bean extract, various botanical extracts for subjective evaluation, etc.) (Ongoing)

Synthetic Chemistry

1. To continue to prepare labelled materials for product-precursor studies within our project as well as satisfying other requests when compatible with current progress. (Ongoing)
2. To complete the preparation, isolation, and characterization of tobacco identical Amadori compounds for product-precursor studies (to be tested subjectively also). (Complete 2nd Quarter)
3. To complete efforts to obtain high specific activity specifically labelled menthol for use in non-destructive tracer work. (Complete 2nd Quarter)
4. To develop a preparation of specifically labelled cellulose for product-precursor studies. (Complete 4th Quarter)

Analytical Chemistry

1. To develop and optimize a suitable gas chromatographic method (probably heart-cutting) for the analysis of radiolabelled compounds (aza-arene, product-precursor studies demanding the ultimate detection limits). (Ongoing)
2. To develop a method for the study of the chemical composition of smoke aerosols. Both GC and HPLC techniques will be utilized. (Ongoing)
3. To develop HPLC methodology for the direct analysis of WSC and selective HPLC techniques for compounds by chemical class. (Ongoing)
4. To develop HPLC and GPC methodology for the study of the transfer of high molecular weight compounds to mainstream smoke (use of characterized polymeric materials). (Ongoing)

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5. To elucidate the mechanism of mainstream/
sidestream partitioning through the use of
pyrolytic precursor-product techniques. (Ongoing)

Smoke Chemistry Modelling Studies

The high temperature interaction between secondary
amines (or secondary amine precursors) and nitrate
and/or nitrite will be studied under conditions
which resemble the burning cigarette. Variations
in conditions such as temperature, pH, catalysts,
and surface conditions will be investigated.
(4th Quarter)

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